



Use and abuse of loperamide . . . and other stories

Loperamide as a drug of abuse

Loperamide is an over-the-counter drug frequently bought to treat travellers' diarrhoea. At therapeutic doses, it exerts its action peripherally through activation of mu-opioid receptors in intestinal tissue. However, at higher doses it can cross the blood-brain barrier and lead to mood changing effects of the sort seen with other mu-opioid agonists such as morphine. Online surveys from the UK and US suggest that non-medical use of loperamide is widespread both for its euphoric properties and to mitigate the unpleasant effects of withdrawal from other opiates (*QJM* doi:10.1093/qjmed/hcz215).

The fragility index

The fragility index has nothing to do with osteoporosis or bony fracture. Rather, it's a measure of the robustness of the results of randomised controlled trials and defined as the minimum number of participants who, if their outcome were switched from non-event to event, would turn a statistically significant result non-significant. An analysis of trials used to support American guidelines on myocardial re-vascularisation found that more than a quarter had a fragility index of 3 or less (*Circulation* doi:10.1161/CIRCOUTCOMES.119.006017). Equally worrying, more than 40% of trials had a fragility index lower than the number of participants lost to follow-up.

Functional cognitive symptoms

A review of nearly 250 studies of people with symptoms of impaired cognition challenges the idea that subjective cognitive symptoms are a precursor of cognitive decline and dementia. On the contrary, it finds that such symptoms are common, that

in many cases they aren't progressive, and that, even after structural and functional imaging, a specific underlying cause often can't be identified. The investigators think that more attention needs to be paid to these functional disorders which, despite their prevalence, rarely feature in dementia research (*Lancet Psych* doi:10.1016/S2215-0366(19)30405-5).

Depression and dementia

On the subject of cognitive function, two large longitudinal studies from Sweden explore links between depression and later dementia, an association that has been noted in numerous observational studies. In both cohorts, the risk of dementia was 10 to 20 times higher in people during the first year after a diagnosis of depression (*PLoS Med* doi:10.1371/journal.pmed.1003016). Risk then decreased rapidly but was still evident more than 20 years later. The findings suggest that depression can be both a long term risk factor for dementia and an early sign of the condition.

Arterial pressure waveforms

The invention of the sphygmomanometer allowed systolic and diastolic blood pressures, the extremes of the arterial pressure waveform, to be measured. The results proved so useful that the rest of the arterial waveform was largely ignored. This may be discarding valuable information. Radial artery recordings from 6000 participants in a longitudinal study from the US were used to develop measures of the rate of pressure decay—an indicator of the elasticity of the arterial side of the circulation (*Am J Epidemiol* doi:10.1093/aje/kwz280). Both these measures were associated with cardiovascular risk independently of traditional risk factors.